REMARKS

Favorable reconsideration of this application as presently amended and in light of the following discussion is respectfully requested.

Claims 1-17 are pending in the present application. The present amendment cancels Claim 18 without prejudice or disclaimer; and amends Claims 1, 14 and 17 without introducing any new matter.

Applicants respectfully request the USPTO to disregard the Amendment filed on September 15, 2008.

In the January 14, 2008 Office Action, Claim 17 was objected to for informalities. Claim 18 was rejected under 35 U.S.C. § 112, first paragraph, as introducing new matter. Claims 1-18 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1-2, 8, and 11-12 were rejected under 35 U.S.C. § 102(e) as being anticipated by Lindsay et al. (U.S. Patent Publication No. 2004/0238379, hereinafter "Lindsay"). Claims 1-9 and 11-12 were rejected as unpatentable under 35 U.S.C. § 103(a) over the reference Lindsay in view of Kariyone et al. (U.S. Patent No. 5,242,793, hereinafter "Kariyone"). Claim 10 was rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone, in further view of Hashimoto (U.S. Patent Publication No. 2001/0024788). Claim 13 was rejected as unpatentable under 35 U.S.C. § 103(a) over the reference Lindsay in view of Kariyone, in further view of Price (U.S. Patent No. 5,805,014). Claims 14-15 were rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone, in further view of Hollis et al. (U.S. Patent No. 5,653,939, hereinafter "Hollis") and Dryja et al. (U.S. Patent No. 5,498,521, hereinafter "Dryja".) Claims 14 and 16 were rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone, in further view of Hollis et al. (U.S. Patent No. 5,653,939, hereinafter "Hollis") and Sorenson (U.S. Patent No. 5,496,699). Claim 17 was rejected under

35 U.S.C. § 103(a) as being unpatentable over Lindsay, in view of Kariyone, in further view of Anderson et al. (U.S. Patent No. 5,922,591, hereinafter "Anderson"). Claim 18 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Lindsay, in view of Kariyone, in further view of Heller et al. (U.S. Patent No. 6,281,006, hereinafter "Heller").

In response to an Amendment filed on July 14, 2008, an Advisory Action issued the same day on July 14, 2008 that upheld the rejections of Claim 1 under 35 U.S.C. § 112, first and second paragraph, and the rejections of the claims under 35 U.S.C. § 103(a), but indicated that the objection of Claim 17 would be overcome.

Accordingly, independent Claim 1 is amended to recite all the features of Applicants' dependent Claim 18. No new matter has been added. Consequently, dependent Claim 18 is cancelled without prejudice or disclaimer. In addition, Claim 1 is amended to recite "fixing a potential of the electrolyte solution which covers said active zones with an electrode ***that operates as a common gate electrode for the field effect transistors***, the electrode immerged in said electrolyte solution." (Claim 1, emphasis added, portions omitted.)

In response to the rejection of dependent Claim 18 under 35 U.S.C. § 112, first paragraph, as introducing new matter, these features now introduced into independent Claim 1, Applicants respectfully traverse this rejection and request reconsideration thereof, as next discussed.

Independent Claim 1 now recites that the electrode "operates as a common gate electrode for the field effect transistors." Applicants respectfully submit that the electrode operating a s common gate electrode for the field effect transistors is clearly described in the disclosure as originally filed.

As can be seen in Applicants' Fig. 1, and as clearly recited in Applicants' specification, the active region 3 between the source S and the drain D of the field effect transistor forms the gate region G, and a thin insulation layer 4 is provided on active region 3.

(See also Specification, p. 5, ll. 23-31.) With respect to Fig. 1, Applicants' specification recites that "[t]he application of a gate-source voltage U_{GS} between the electrolyte 6 and the source S (for example by means of a single Ag/AgCl electrode E) induces a two dimensional gas of charge carriers at the $Si/Si0_2$ interface, or at the Si/electrolyte interface of each resistor." (Specification, p. 6, ll. 6-12.) The measuring solution 6 covers the gate regions G of the transistors, and the electrode E that is immerged in the electrolyte solution 6 fixes the potential of the electrolyte solution as well as the gate voltage of the transistors, to set the operation point of the sensors that include the transistors. (Specification, p. 7, ll. 10-20.) In addition, in Fig. 1 it can be seen that the voltage between electrode E and source S has been named U_{GS} for a gate-source voltage.

In view of the above discussion, it is clear that electrode E forms a gate electrode for the transistors. It is believed that the rejection of the features of Claim 18 under 35 U.S.C. § 112, first paragraph, is overcome.

In response to the objection to Claim 17 and the rejection of Claims 1 and 16 under 35 U.S.C. § 112, second paragraph, Claim 17 is amended to recite "at least one field-effect transistor." Moreover, Claim 1 is amended to recite that "at least two of the field-effect transistors having at least two active zones that are part of said some of active zones, corresponding to a first group," and Claim 14 is amended to recite that the first and second enzymological reaction are performed in the first and second zones, respectively. In view of amended Claims 1 and 14, it is believed that all pending claims are definite and no further rejection on that basis is anticipated. If, however, the Examiner disagrees, the Examiner is invited to telephone the undersigned who will be happy to work with the Examiner in a joint effort to derive mutually acceptable language.

In response to the rejection of Claim 18 under 35 U.S.C. § 103(a), the features of dependent Claim 18 now incorporated into independent Claim 18, Applicants respectfully requests reconsideration of this rejection and traverse the rejection, as discussed next.

Briefly summarizing, Applicants' amended independent Claim 1 is directed to a method for detecting at least one parameter representative of molecular probes fixed to active zones of a sensor, wherein said sensor includes a network of field-effect transistors, each of which has a source region, a drain region, and a gate region which forms one of said active zones on which said representative parameter is detected. The method includes *inter alia* the steps of: bringing some of said active zones into contact with molecular probes in order to fix said probes; bathing at least said some of active zones which have been brought into contact with said molecular probes, in an electrolyte solution; measuring at least one point of at least one of a drain current, source-gate voltage, and source-drain voltage characteristic of at least two of the field-effect transistors, so as to deduce therefrom at least one said representative parameter ***by comparison between at least two measurements obtained for two different active zones*** immerged in said electrolyte solution, and ***fixing a potential of the electrolyte solution which covers said active zones with an electrode that operates as a common gate electrode for the field effect transistors, the electrode immerged in said electrolyte solution***.

The advantages of Applicants' independent Claim 1 in light of the specification are next discussed. By making comparative or differential measurements between conventional FET transistors having a same gate voltage as well as the same voltage for the electrolyte solutions, the features of Applicants' Claim 1 allow making significant measurement improvements, by considerably increasing the sensitivity of a comparative or differential measurement. As explained in Applicants' specification at p. 7, ll. 10-20, with electrode E in the electrolyte solution, the voltage of the gates and of the electrolyte solution is no longer

floating and is held at the same level, which avoids noise for a comparative or differential measure. Furthermore, as shown in Applicants' Fig. 8A-8C, the differential measurement shows current differences around 10 μA for drain current (Fig. 8A), or 150 mV for source-gate voltage (Fig. 8C), and about 60 mV for source gate voltage (Figs. 9C-9D). Please note that the above discussion is for explanatory purposes only, and is not intended to limit the scope of the claims in any fashion.

The reference Lindsay is directed to a method for electronically detecting hybridization of a probe nucleic acid and a target nucleic acid, (Lindsay, Abstract) and the reference Kariyone is directed to a selectively permeable membrane that is disposed on an electrode. (Kariyone, Abstract.)

However, the pending Office Action confirms that both Lindsay and Kariyone fail to teach "fixing the potential of the active zones." However, the pending Office Action believes that the reference Heller teaches such a feature in his columns 2 and 5, and assumes that the combination of Lindsay with Kariyone is proper. Applicants respectfully disagree with these assertions, as next discussed.

First, amended, independent Claim 1 now requires "fixing a potential of the electrolyte solution which covers said active zones with an electrode that operates as a common gate electrode for the field effect transistors, the electrode immerged in said electrolyte solution." Just like Lindsay and Kariyone, the reference Heller fails to teach such a feature. Heller is directed to an electrochemical affinity assay system to detect ligand-ligand receptor bindings. (Heller, Abstract.) The system includes a working electrode 10 coated with a redox polymer 12, in which the first member 14 is immobilized via a binding agent 11. (Heller, col. 3, ll. 60-65, Fig. 1A.) Heller explains that the working electrode 10 is countered by a counter electrode, so that an electrical field is created between electrode 10 and the counter electrode. (Heller, col. 4, ll. 38-49, col. 5, ll. 43-50.) However, Heller fails

to teach fixing a potential of the electrolyte solution which covers said active zones with an electrode that operates as a common gate electrode for the field effect transistors, the electrode immerged in said electrolyte solution, as required by Applicants' amended independent Claim 1. Heller merely mentions an electrode that forms a capacitor to create an electrical field together with a counter electrode. Heller does not use any transistors at all.

Second, Applicants respectfully traverse the obviousness of the combination between Lindsay and Heller, because there is no articulated reasoning provided by the pending Office Action for the obviousness, nor is there any motivation to perform such combination, as next discussed.[1]

The reference Lindsay is directed to a method for electronically detecting hybridization of a probe nucleic acid and a target nucleic acid. (Lindsay, Abstract.) For his method, Lindsay explains that a back-gated field effect transistor FET is used, where a layer of silicon 10 is provided on a buried oxide layer 20, located on a silicon wafer 30, where a source 40 and drain 50 and a n-channel 65 are provided in the silicon 10. (Lindsay, p. 2, ¶¶ [0019]-[0020], Fig. 1a.). A fluid placed on or in an upper surface 75 of n-cannel 65 the semiconductor can be charged to interact with the semiconductor. (Lindsay, p. 3, ¶ [0028], Figs. 1a, 1b). Lindsay also explains that when the FET is operated with a buffer including a DNA on the channel 65 for a measurement, an applied drain-source bias voltage 70 is kept constant, and a backgate voltage 60 V_{bg} is grounded. (Lindsay, p. 4, ¶ [0036]-[0037], Fig. 7.)

In contrast, the reference Heller is directed to an assay system, where an electrical field is generated between two electrodes, where a working electrode 10 is deposited on an insulating substrate and a counter electrode. (Heller, col. 4, ll. 50-57 and col. 5, ll. 43-59.) By creating a sandwich assay structure by employing a simultaneous binding between members 11, 14, 16, 18 and 20, the system can generate an electrical current between the

[1] KSR v. Teleflex, 550 U.S. ___, 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385 (2007)

working electrode 10 and the counter electrode. The conduction relies on an electrochemical reaction mediated by member 18, 20, and the substrate generating enzyme. (Heller, col. 4, ll. 3-24.)

The pending Office Action asserts that the combination of Lindsay and Heller is obvious "to have modified the method comprising additional gate electrodes not used for hybridization as taught by Lindsay et al in view of Kariyone et al with the single combination counter and reference electrode on the array that fixed the potential as taught by Heller et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of a minimal number of structures used in the method as a result of having a single electrode that serves all of the electrodes of the array as explicitly taught by Heller et al (column 4, ll. 40-60)." (Office Action, starting on p. 18, l. 22.)

Applicants respectfully disagree with these assertions, because the disclosures Lindsay and Heller are substantially different: while Lindsay's system is based on the n-channel inversion layer 65 between an n-type source 40 and a n-type drain 50 of a field effect transistor (FET), Heller's assay system is based on an electrical field of a capacitor formed by electrode 10 and a counter electrode. Heller simply measures an electrical current flow between two electrodes, as discussed above. Despite the explanations provided by the pending Office Action, it is not clear how electrodes of a capacitor of Heller could be incorporated into Lindsay's channel inversion layer 65 of a FET. Such modification would change the basic principle of operation of Lindsay. There is no evidence that a person of ordinary skill in the art would be motivated to perform such changes and redesign.[2]

[2] See In re Ratti, 270 F.2d 810, 813, 123 USPQ 349, 352 (reversing an obviousness rejection where the "suggested combination of references would require a substantial reconstruction and redesign of the elements shown in [the primary reference] as well as a change in the basic principle under which the [primary reference] construction was designed to operate.")

Accordingly, Applicants respectfully submit that not only does the combination of Lindsay, Kariyone and Heller fail to teach all the features of Applicants' independent Claim 1, but also it is believed that the combination of these references is not obvious. Therefore, Applicants respectfully traverse the rejection, and request reconsideration thereof.

Consequently, in view of the present amendment, no further issues are believed to be outstanding in the present application, and the present application is believed to be in condition for formal Allowance. A Notice of Allowance for Claims 1-17 is earnestly solicited.

Should the Examiner deem that any further action is necessary to place this application in even better form for allowance, the Examiner is encouraged to contact Applicants' undersigned representative at the below listed telephone number.

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